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One-Pot Suzuki-Hydrogenolysis Protocol for the Modular Synthesis of 2,5-Diaryltetrazoles

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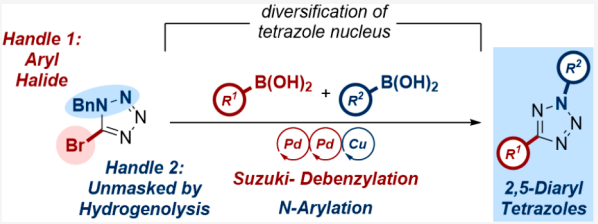
ABSTRACT: 2,5-Diaryltetrazoles are a diverse range of compounds of considerable interest within the field of photochemistry as a valuable precursor of the nitrile imine 1,3-dipole. Current literature approaches toward this heterocycle remain unsuitable for the practical synthesis of a library of these derivatives. Herein, we disclose the development of a modular approach toward 2,5-diaryltetrazoles compatible with an array-type protocol, facilitated by a tandem Suzuki-hydrogenolysis approach.



INTRODUCTION

The recent resurgence of photochemistry as a unique and powerful method of forging and manipulating C−C bonds has stimulated the development and adaption of numerous synthetic protocols.[1] One such transformation is the photolysis of the 2,5-diaryltetrazole moiety to yield the versatile nitrile imine 1,3-dipole (Scheme 1a).[2−4] Owing to its facile reactivity with a number of functional groups including alkenes[4b,5] and carboxylic acids,[6] the nitrile imine has recently found widespread application in fields where an orthogonal reactivity profile (click chemistry[7]) is desirable, such as materials chemistry and chemical biology.[8,9]

Due to the traceless reaction profile and inherent simplicity of photolyzing tetrazole systems, this protocol has become the most common method of nitrile imine generation. However, synthetic approaches toward 2,5-tetrazoles are limited relative to the requirement for structural diversity from the corresponding dipole precursors. In our laboratories, we were interested in the synthesis of a small library of 2,5-diaryltetrazoles[10] and were surprised to find that the majority of recent reports on the preparation of these compounds rely on a cycloaddition-mediated approach reported by Kakehi (Scheme 1b) over 40 years ago.[11] While this robust synthesis is compatible with a range of substrates, it also typically employs hazardous reagents and often laborious purification protocols. An alternative approach was introduced by Liu in 2015; however, this route is somewhat limited by the commercial availability of the requisite aryl amidines.[12] The continuing limitation in the synthesis of these heterocycles appears to be simultaneous modification of both the *N*- and *C*-aryl rings of the tetrazole. Multiple procedures for the diversification of 5-aryltetrazoles with a palette of *N*-aryl groups have been developed;[13] however, modification of the *C*-aryl ring itself is primarily restricted to classical syntheses via cycloaddition between the relevant benzonitrile and hydrazoic acid (Scheme 1b).[14] This approach again requires use of toxic and explosive reagents. More recently, Kamenecka disclosed a route toward 2-aryl-5-bromotetrazoles; however, this also requires the use of hazardous reagents, and subsequent derivatization to furnish *C*-aryl functionalized systems was not conducted.[15]

While the existing approaches are well-suited to the focused synthesis of specific 2,5-diaryltetrazole species, we found most methods incompatible with an array-type approach toward a library of such compounds. We envisioned that a common intermediate containing the preformed tetrazole nucleus encoded with chemoselective functional handles would allow for simple, rapid modification of both the 2- and 5-positions of the heterocyclic ring system.

The use of 1-benzyl-5-bromotetrazole (**1**) as a starting material fulfilled all of the requirements discussed above for a facile and robust synthesis of tetrazole systems ready for further functionalization (Scheme 1c). Given our laboratory's previous efforts in the development of a tandem Suzuki-hydrogenation protocol in the synthesis of sp^3-rich pharmaceutical building-blocks,[16] we reasoned that the treatment of **1** to similar conditions would facilitate modification of the 5-position, while simultaneously unmasking the 2-position for derivatization using existing literature methodology.[13c] Furthermore, **1** itself could be easily accessed on scale by alkylation and bromination of 1*H*-tetrazole, a commodity precursor, obviating the need for the hazardous synthesis of the heterocyclic constituent.

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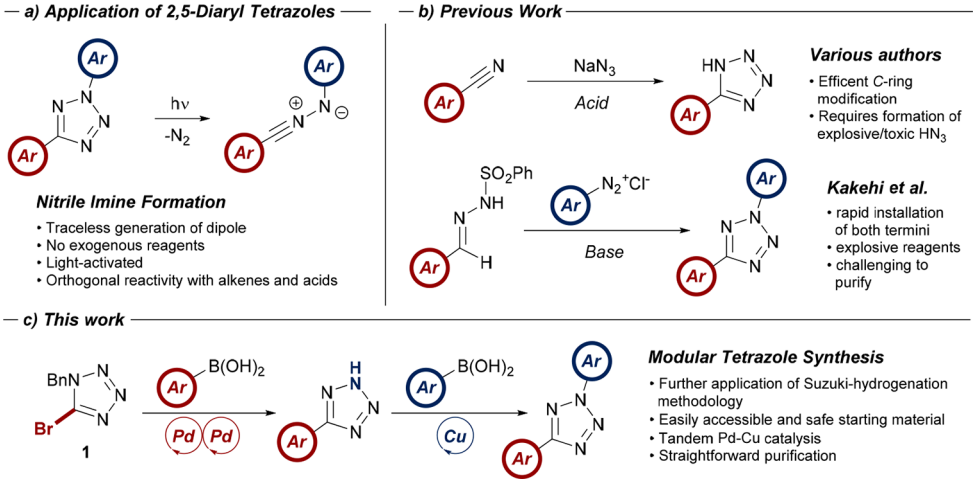
Scheme 1. (a) Application of 2,5-Tetrazoles as a Nitrile Imine Source; (b) Previous Efforts toward the Synthesis of Functionalized Tetrazoles; (c) This Work: Modular Synthesis of 2,5-Diaryltetrazoles via a Two-Step Tandem Pd and Cu Catalysis Approach



RESULTS AND DISCUSSION

The current study commenced with the investigation of the initial Suzuki coupling between **1** and aryl boronic acids. An initial literature search identified conditions reported by Yi in the coupling of similar substrates, using $Pd(PPh_3)_4$ as a catalyst.[17] As the presence of the triphenylphoshine ligand has previously been shown to be detrimental in one-pot Suzuki-hydrogenation methodology,[16] we sought to identify a suitable replacement Pd complex. Our optimization campaign began with the screening of six palladium precatalysts in combination with a number of different solvents and bases (Figure 1).

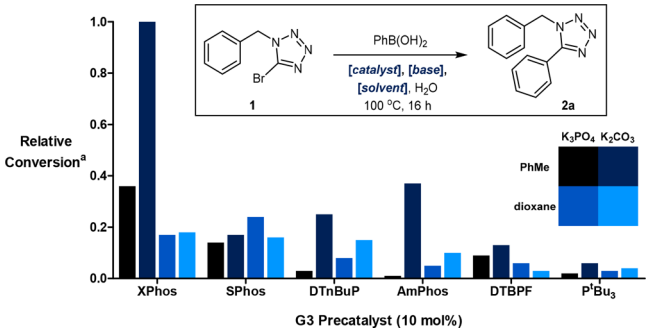
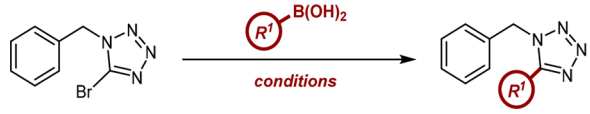


Figure 1. Initial catalyst screening identified XPhos Pd G3 as a suitable candidate for further study. [a] Conversion was determined by HPLC with reference to an internal standard. All reactions were performed on a 2.5 μmol scale using 1.5 equiv of $PhB(OH)_2$, 2 equiv of base, and a 4:1 solvent/H_2O ratio (0.8 M).

XPhos Pd G3 was quickly identified as a potential alternative catalyst. When employed in conjunction with toluene, these reaction conditions afforded a substantially greater conversion than all other combinations examined.

Gratifyingly, a direct comparison between the previously reported conditions and this emerging approach furnished nearly identical yields (Table 1, entries 1 and 2). Furthermore, this was accomplished over a much shorter time frame of 3 h; however, the catalyst loading remained higher. Both electron-donating and mildly electron-deficient boronic acids were shown to be compatible substrates (Table 1, entries 3 and 4); however, 4-cyanophenylboronic acid proved recalcitrant to

Table 1. Direct Comparison between Established Literature Precedent and the Newly Identified Reaction Conditions



entry	R^1	conditions	isolated yield (%)
1[a]	Ph	$Pd(PPh_3)_4$ (3 mol %), Na_2CO_3, PhMe, EtOH, H_2O, 110 °C, 16 h[17]	75
2[b]	Ph	XPhos Pd G3 (10 mol %), K_2CO_3, PhMe, H_2O, 100 °C, 3 h	76
3[b]	4-(MeO) $PhB(OH)_2$	as above	72
4[b]	4-(F) $PhB(OH)_2$	as above	60
5[b]	4-(NC) $PhB(OH)_2$	as above	trace

[a]Performed on a 1 mmol scale using 1.3 equiv of $PhB(OH)_2$, 2 equiv of Na_2CO_3, and 50 equiv of H_2O at a concentration of 0.1 M. [b]Performed on a 0.25 mmol scale using 1.5 equiv of $PhB(OH)_2$, 2 equiv of K_2CO_3, and 100 equiv of H_2O at a concentration of 0.1 M.

product formation (Table 1, entry 5). In an effort to determine the compatibility of strongly electron-deficient boron species within the reaction manifold, a second screening effort was conducted, using an array of relevant variables selected based on the results of the initial screen (Figure 2). These results suggested that while the nitrile derivative remained intolerant to the reaction conditions, the improved performance of 4-(trifluoromethyl)-phenylboronic acid indicated that this issue was substrate-specific, rather than a consequence of electronic factors. Throughout this additional screen, XPhos was again shown to represent the most favorable precatalyst, while cesium was identified as the carbonate counterion.

With optimal discrete variables in hand, we turned our attention to the catalyst loading. Preliminary efforts proved frustrating, with a significant decrease in yield observed upon reduction of catalyst loading (Table 2, entries 1−3). However, a concurrent Design of Experiments study[18,19] highlighted an unanticipated correlation between the water stoichiometry of the reaction, relative to the overall concentration, and the

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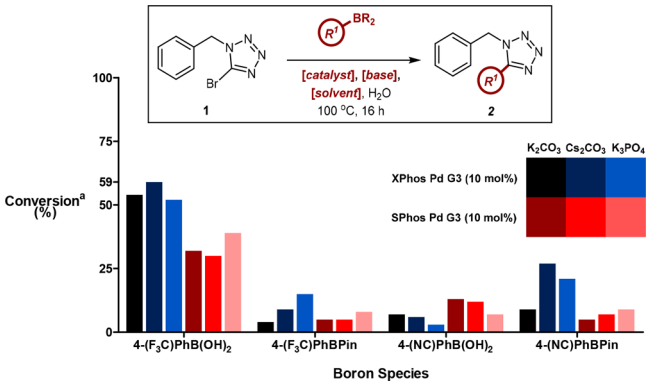
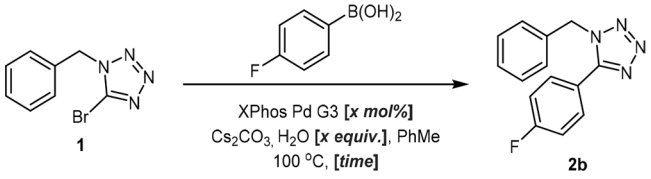


Figure 2. Additional screen of electron-deficient boron species indicated that some substrates were compatible with the conditions, while Cs_2CO_3 represented a minor improvement over K_2CO_3. [a] Conversion was determined by LCMS with reference to caffeine as an internal standard. All reactions were performed on a 50 μmol scale using 1.5 equiv of $PhB(OH)_2$, 2 equiv of base, and 50 equiv of H_2O at a concentration of 0.1 M.

Table 2. Minimization of Catalyst Loading through Manipulation of Water Stoichiometry[a]



entry	catalyst loading (mol %)	H_2O stoichiometry (equiv)	time (h)	conversion[b] (%)
1	10	10	16	52
2	5	10	16	47
3	2.5	10	16	14
4	10	100	4	70
5	5	100	4	71
6	4	100	4	70
7	**3**	**100**	**4**	**71**
8	2	100	4	66
9	1	100	4	38

[a]Reactions performed on a 50 μmol scale using 1.3 equiv of $PhB(OH)_2$ and 1.5 equiv of Cs_2CO_3 at a concentration of 0.1 M. [b]Conversion was determined by LCMS with reference to caffeine as an internal standard.

observed conversion (Figure 3, see the Supporting Information for full details). Exploiting this finding successfully furnished the optimized reaction conditions for the Suzuki component of the proposed process, with a catalyst loading of 3 mol % (Table 2, entries 4–9).

Studies into the subsequent debenzylation protocol proved to be more straightforward. A screen of eight Pd/C catalysts from three different sources afforded in many cases examples of quantitative conversion, with ethanol identified as an appropriate solvent (Figure 4). Further investigations highlighted Evonik's Noblyst P1071 Pd/C catalyst as a desirable option to mediate the transformation (see the Supporting Information for further details). A final optimization found that a 2.5 mol % loading of catalyst facilitated quantitative conversion under only 4 bar of hydrogen gas (Table 3, entries 1–3). It was also determined that gentle heating of the

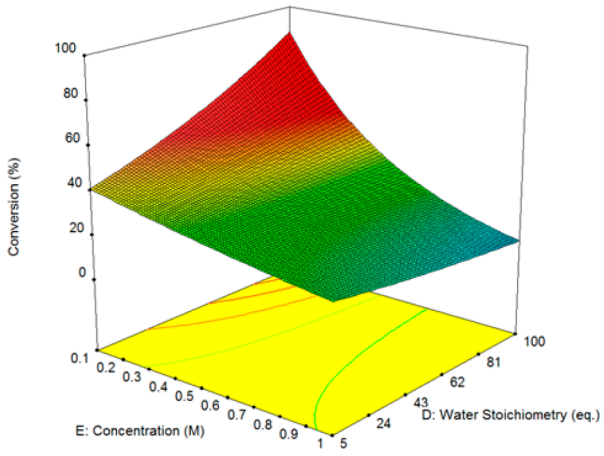


Figure 3. Response surface from the Design of Experiments study that revealed the importance of water stoichiometry to conversion through a secondary correlation with overall reaction concentration. See the Supporting Information for full details.

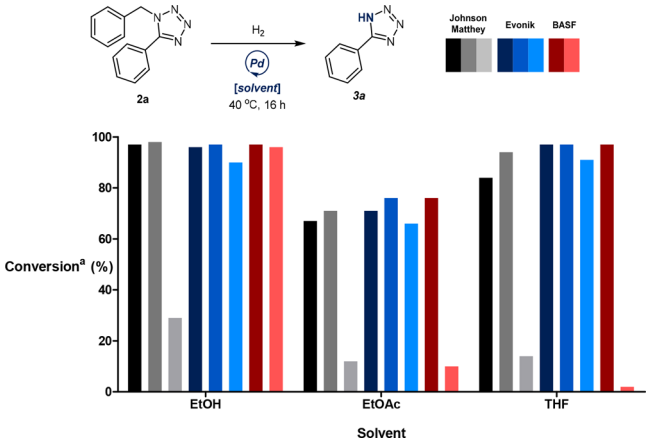


Figure 4. Preliminary screening of Pd/C catalysts generated a high degree of success. (a) Conversions reported as a percentage of the total peak area of **2a** and **3a**. All reactions were performed on a 63 μmol scale using 6 bar of H_2 and 30 wt % of Pd/C at a concentration of 0.17 M.

reaction mixture to 40 °C was essential for enabling full conversion (Table 3, entry 4).

Translation of this methodology into a one-pot procedure proved challenging, with preliminary attempts affording only moderate turnover. Gratifyingly, further reducing the pressure of hydrogen gas was found to increase this yield to synthetically useful levels (Table 4, entries 1 and 2). Consistent with our previous work,[16] the catalyst ratio was found to be a crucial factor in maximizing product formation. While the isolated debenzylation conditions required only a 2.5 mol % Pd/C loading, any reduction below 10% Pd/C significantly impacted conversion within the one-pot manifold (Table 4, entry 3). Attempts to circumvent the addition of ethanol as a cosolvent at the midpoint of the reaction also failed to furnish improved conversions (Table 4, entries 4–6). However, satisfactory conditions were identified with a total Pd catalyst loading of 13 mol %, furnishing a 65% isolated yield of **3a** in 22 h.

With fully optimized reaction conditions in hand, we next sought to investigate the scope of this one-pot procedure with respect to the boronic acid substituent (Table 5a).

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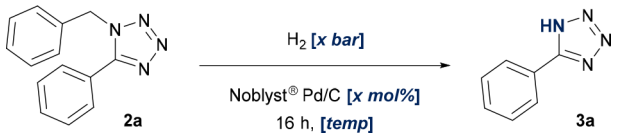
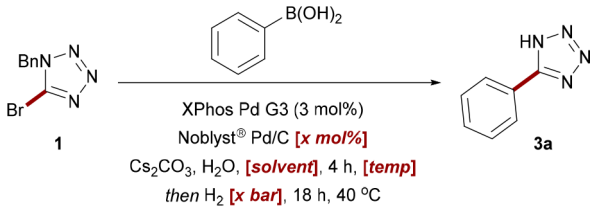
Table 3. Further Optimization of Hydrogenolysis Conditions



entry	H_2 pressure (bar)	Pd/C loading (mol %)	temp (°C)	conversion[d] (%)
1[a]	6	7	40	97
2[b]	4	5	40	98
3[b]	**4**	**2.5**	**40**	**99**
4[c]	4	2.5	rt	59

[a]Performed on a 63 μmol scale at a concentration of 0.17 M. [b]Performed on a 127 μmol scale at a concentration of 0.17 M. [c]Performed on a 0.3 mmol scale at a concentration of 0.1 M. [d]Conversions were determined by LCMS with reference to caffeine as an internal standard.

Table 4. Optimization of One-Pot Reaction Conditions[a]



entry	H_2 pressure (bar)	Pd/C loading (mol %)	solvent	temp (°C)	conversion[b] (%)
1	4	10	PhMe[c]	100	43
2	**2**	**10**	**PhMe**[c]	**100**	**65 (65)**[d]
3	2	5	PhMe[c]	100	34
4	2	10	PhMe	100	24
5	2	10	4:1 PhMe:*n*BuOH	100	24
6	2	10	4:1 PhMe:EtOH	70	37

[a]Reactions performed on a 0.5 mmol scale using 1.3 equiv of $PhB(OH)_2$, 1.5 equiv of Cs_2CO_3, and 100 equiv of H_2O at a concentration of 0.1 M. [b]Conversions were determined by LCMS with reference to caffeine as an internal standard. [c]EtOH (2.5 mL) was added as a cosolvent prior to the hydrogenolysis step of the reaction. [d]Isolated yield.

Introduction of electronically deficient and neutral moieties were found to be well-tolerated, with minimal impact on yield (cf. **3b**–**3d**). Similarly, *meta*- and *ortho*-substitution of the aryl component was found to be compatible (cf. **3e** and **3f**), although the reduced yield of the *meta* analogue **3e** remains more difficult to rationalize. More sterically encumbered substrates **3g** and **3h** were also successfully isolated. The modest yield associated with **3h** can likely be attributed to the increased size of the tetrazole hindering adsorption of the substrate onto the surface of the Pd/C catalyst. Reaction conditions were also found to be amenable to scale-up, with substrates **3a**, **3b**, **3f**, and **3g** successfully synthesized in good yield on a 2.5 mmol scale.

While the one-pot generation of 5-aryltetrazoles is preferable from a practical perspective, the yields of certain substrates were found to benefit from a directly related two-pot procedure (Table 5b). This approach enabled the robust synthesis of electron-rich analogue **3i**, a key pharmacophore of a reported allosteric potentiator of the metabotropic glutamate 2 receptor.[20] Vinyl boronic acids were also found to be compatible, with the synthesis of **3j** in good yield, providing access to alkyl tetrazole derivatives via a formal sp^2–sp^3 coupling. Biaryl substrates **3k** and **3l** represent examples of an important subset of nitrile imine precursors with extended π-systems with a diminished yield in the case of the bulkier *o*-phenyl species. While low-yielding, methoxy ester substrate **3m** provides a valuable functional handle for further derivatization. To exhibit the versatility of this procedure, the debenzylation step of this scope exploited the ex situ generation of H_2 gas in a two-chambered reaction vessel known as COware,[21] attaining the required pressure of H_2 without the need for more specialized apparatus.

To further exemplify the advantages afforded by this modular approach, we targeted the synthesis of a diverse matrix consisting of 16 2,5-diaryltetrazoles (Table 6). *N*-Aryl substituents were selected on the basis of their unique influence on the properties of the resulting heterocycle, such as the incorporation of a handle for further covalent modification (e.g., **4f**) or the manipulation of λ_{max} properties (e.g., **4k**). The current approach was found to be highly effective, with the synthesis of 15 of the 16 tetrazoles accomplished in good to excellent yields in conjunction with the established copper-mediated *N*-arylation protocol.[13c] The practicality of this approach represents a significant advance over existing methods in the synthesis of a diverse library of nitrile imine precursors. One of the most beneficial aspects is the absence of time-consuming purification procedures. Owing to the acidic character of **3**, appropriate moderation of pH during reaction workup afforded all 5-aryl-1*H*-tetrazoles at a sufficient level of purity for subsequent manipulation without the need for additional decontamination. Commencing from 5-bromotetrazole **1**, the synthesis of 2,5-tetrazoles **4a**–**p** required only one chromatographic purification step prior to the isolation of the final product. The synthesis of tetrazole **4a** on a 6 mmol also demonstrated the scalability of the procedure, meaning that the entire route was shown to afford an overall yield of greater than 50% on a multimillimolar scale. The unexpected failure of substrate **4j** can be perhaps be attributed to a lower thermal stability of the tetrazole due to the enhanced push–pull system generated by the substituents.[22]

CONCLUSIONS

In conclusion, we have developed a convenient and widely applicable Suzuki-hydrogenolysis protocol enabling the expedient synthesis of 2,5-diaryltetrazoles, valuable precursors of the nitrile imine 1,3-dipole. The scope of the reaction was shown to be tolerant of a range of steric and electronic parameters and was further expanded through the accommodation of a hyphenated, two-pot procedure. Facile synthesis of a diverse palette of 2,5-tetrazoles in combination with existing Cu-catalyzed methodology has underlined the utility of this reaction, which offers a complementary means of accessing the 2,5-diaryltetrazole scaffold in comparison to previous reports. We intend to further utilize this transformation in our continued investigations into the reactivity of the pleiotropic nitrile imine dipole.

EXPERIMENTAL SECTION

General Information. All reagents and solvents were obtained from commercial suppliers and were used without further purification

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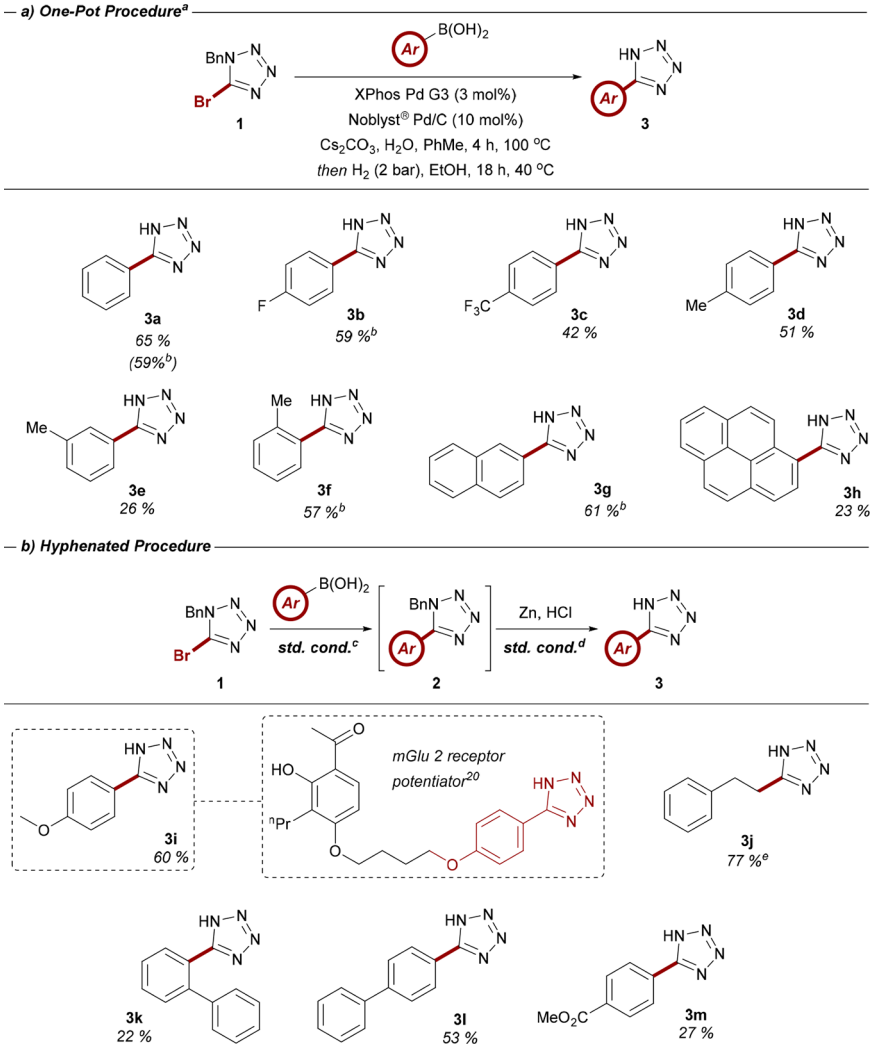
Table 5. (a) Exemplar Scope of Aryl Boronic Acids Compatible with the One-Pot Suzuki-Hydrogenolysis Coupling Protocol; (b) Library of Boronic Acids Employed as Part of the Hyphenated Two-Pot Synthesis of 5-Aryltetrazoles



[a]Reactions performed on a 0.5 mmol scale using 1.3 equiv of boronic acid, 1.5 equiv of Cs_2CO_3, and 100 equiv of H_2O at a concentration of 0.1 M. [b]2.5 mmol scale. [c]1 equiv of **1**, 1.5 equiv of boronic acid, 2 equiv of Cs_2CO_3, 3 mol % of XPhos Pd G3, and 10 equiv of H_2O, heated at 100 °C in a solution of PhMe (0.2 M) for 2 h. [d]1 equiv of **3** and 10 mol % of Noblyst Pd/C, heated at 40 °C in a solution of EtOH (0.1M) for 18 h in the presence of 2 bar H_2 generated from Zn and HCl. [e]From (*E*)-styrylboronic acid.

unless otherwise stated. Purification was carried out according to standard laboratory methods. All reactions were conducted using round-bottom flasks or microwave vials of appropriate volume, unless otherwise stated. Reactions were carried out at elevated temperatures using a temperature-regulated hot plate/stirrer with a sand bath unless otherwise stated. Phase separation was conducted using IST Isolute Phase Separator Cartridges.

Flash chromatography was carried out manually using ZEOprep 60 HYD 40−63 μm silica gel or using a Teledyne ISCO CombiFlashRF+ apparatus with RediSep silica cartridges.

Fourier transform infrared (FTIR) spectra were obtained using a PerkinElmer Spectrum One Fourier Transform spectrometer with samples used neat. ^{1}H, ^{19}F, and ^{13}C NMR spectra were obtained on a Bruker DRX 500, Bruker AVI, or Bruker Nano spectrometer at 400 or 500, 471 or 376, and 100 or 126 MHz, respectively. Chemical shifts are reported in ppm and coupling constants are reported in Hz with $CDCl_3$ referenced at 7.26 (^{1}H) and 77.16 ppm (^{13}C) and DMSO-d_6 referenced at 2.50 (^{1}H) and 39.52 ppm (^{13}C). Signal assignment of novel compounds was instructed using relevant 2D NMR experiments. High-resolution mass spectra were obtained on a Waters XEVO G2-XS QTof instrument (100−1200 AMU) in positive ionization mode. Reversed-phase HPLC data was obtained using a Waters CSH C18 column. LCMS spectra were obtained using an Acquity UPLC CSH C18 column (50 mm × 2.1 mm i.d. 1.7 μm packing diameter) at 40 °C. The solvents employed were a 0.1% v/v solution of formic acid in water and a 0.1% v/v solution of formic acid in acetonitrile. The UV detection was a summed signal from wavelengths 210 nm −360 nm. Mass spectral data was acquired using a Waters QDA instrument (100−1000 AMU at 5 Hz) with an alternate-scan positive and negative electrospray ionization mode.

HPLC analysis was performed using a gradient method, eluting with 5−90% MeCN/H_2O over 1 min at a flow rate of 1 mL/min when employing standalone HPLC, and eluting with 3−98% MeCN/H_2O (+ formic acid modifier) over 2 min at a flow rate of 1 mL/min when used in conjunction with MS. Reactions using an internal standard required prior HPLC calibration using samples containing varying molarities of product and caffeine, allowing calculation of the response factor by substituting values into eq 1. Screening reactions were then conducted using a known molarity of caffeine internal standard.

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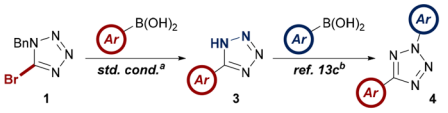
Table 6. Synthesis of a Matrix of 2,5-Diaryltetrazoles Facilitated by Novel Suzuki-Hydrogenolysis Methodology[a]



Ar		NHAc		Me
	4a[c] 54 %[d] (83 %)[e]	4b 54 % (83 %)	4c 55 % (84 %)	4d 51 % (78 %)
F	4e 46 % (78 %)	4f 42 % (71 %)	4g 9 % (15 %)	4h 48 % (81 %)
	4i 52 % (85 %)	4j n.r.	4k 10 % (16 %)	4l 21 % (35 %)
Me	4m 39 % (68 %)	4n 40 % (71 %)	4o 17 % (30 %)	4p 36 % (63 %)

[a]Reactions performed on a 0.5 mmol scale using the conditions described in Table 5a. [b]Reactions performed on a 0.20−0.25 mmol scale. [c]*N*-Arylation was also performed on a 6 mmol scale in an 88% yield. [d]Overall yield. [e]Yield of the individual *N*-arylation step.

$$\text{response factor} = \frac{\left(\frac{\text{area}}{\text{molarity}}\right)\text{product}}{\left(\frac{\text{area}}{\text{molarity}}\right)\text{standard}} \quad (1)$$

General Procedure for the Synthesis of Compounds 3a−3h. To a 10 mL Biotage Endeavor reaction vessel was added Evonik Noblyst P1071 20% palladium on carbon (10 mol %). 1-Benzyl-5-bromo-1*H*-tetrazole (**1**, 1 equiv), an aryl boronic acid (1.3 equiv), and XPhos Pd G3 (3 mol %) were then added as a solution in toluene (0.1 M). To the resulting suspension was added cesium carbonate (1.5 equiv) as a solution in water (100 equiv), at which point the vessel was purged with nitrogen and stirred at 100 °C for 4 h. Upon cooling to room temperature, ethanol (50% volume of toluene) was added before the vessel was placed under a hydrogen atmosphere and heated at 40 °C for a further 18 h. Upon reaction completion, the mixture was passed through Celite and partitioned between ethyl acetate (30 mL) and water (30 mL). The organic phase was washed twice more with water (2 × 30 mL) before the aqueous phases were combined and acidified using 2 M HCl solution (20 mL). The acidic aqueous phase was then washed three times with ethyl acetate (3 × 30 mL) before all organic layers were then combined, passed through a phase separator, and concentrated under reduced pressure to yield the product.

General Procedure for the Synthesis of Compounds 3i−3m. To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (**1**, 1 equiv), an aryl or vinyl boronic acid (1.5 equiv), and XPhos Pd G3 (3 mol %) was added toluene (0.2 M). The vessel was purged with nitrogen, and cesium carbonate (2 equiv) and water (10 equiv) were added. The mixture was stirred at 100 °C for 2 h before being cooled to room temperature. The mixture was diluted with ethyl acetate (10 mL) and passed through a Celite plug, which was then washed with a further portion of ethyl acetate (10 mL). The solution was concentrated under reduced pressure and purified by column chromatography. Isolation of the intermediate 1-benzyl-5-aryltetrazole was confirmed by ^{1}H NMR spectroscopy before the species was added to chamber A of a 2 × 10 mL COware reaction vessel[21a] as a solution in ethanol (0.1 M). Evonik Noblyst P1071 20% palladium on carbon (10 mol %) was also added to chamber A, while chamber B was charged with zinc powder (1.8 mmol, 118 mg) and 36% hydrogen chloride solution (343 μL, 4 mmol). The vessel was sealed and stirred at 40 °C for 18 h. The mixture was cooled to room temperature, diluted with ethyl acetate (10 mL) and passed through a Celite plug, which was washed with a further portion of ethyl acetate (10 mL). This organic phase was washed twice with water (2 × 30 mL), before the aqueous phases were combined and acidified using 2 M HCl solution (20 mL). The acidic aqueous phase was then washed three times with ethyl acetate (3 × 30 mL), before all organic layers were then combined, passed through a phase separator and concentrated under reduced pressure to yield the product.

General Procedure for the N-Arylation of 5-aryltetrazoles. In accordance with previous literature precedent,[13c] 5-aryltetrazole (**3**,1 equiv), an aryl boronic acid (2 equiv), copper(I) oxide (5 mol %), and DMSO (0.13 M) were added to a microwave vial. The reaction mixture was stirred under an oxygen atmosphere at 100 °C for 16 h. The solution was cooled to room temperature and partitioned between ethyl acetate (20 mL) and 1 M HCl solution (20 mL). The aqueous layer was backwashed with an additional portion of ethyl acetate (20 mL) before the combined organic layers were combined, washed with brine (40 mL), passed through a phase separator and concentrated under reduced pressure. The crude product was then purified by column chromatography.

Synthesis and Characterization of Compounds 2-4. *1-Benzyl-5-phenyl-1H-tetrazole (2a).* To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.25 mmol), phenylboronic acid (45.7 mg, 0.38 mmol), and XPhos Pd G3 (21.2 mg, 0.025 mmol) was added toluene (2.0 mL). The vessel was purged with nitrogen, and potassium carbonate (69.1 mg, 0.5 mmol) was added as a solution in water (0.5 mL). The mixture was stirred at 100 °C for 3 h before being cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through Celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (12 g silica cartridge, 0−100% EtOAc in hexane) to give 1-benzyl-5-phenyl-1*H*-tetrazole (45.2 mg, 0.19 mmol, 76% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59−7.52 (m, 3H), 7.51−7.45 (m, 2H), 7.36−7.30 (m, 3H), 7.16−7.11 (m, 2H), 5.61 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 134.0, 131.4, 129.3, 129.2, 128.9, 128.8, 127.3, 123.9, 51.5. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{13}N_4$ 237.1140, found 237.1142. IR ν_{max} (neat): 3065, 3033, 2937, 2857, 1529, 1497, 1458, 1401 cm^{-1}. Analytical data are in agreement with the literature.[17]

1-Benzyl-5-(4-fluorophenyl)-1H-tetrazole (2b). To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.25 mmol), (4-fluorophenyl)boronic acid (52.5 mg, 0.38 mmol), and XPhos Pd G3 (21.2 mg, 0.025 mmol) was added toluene (2.5 mL). The vessel was purged with nitrogen, and potassium carbonate (69.1 mg, 0.5 mmol) and water (0.045 mL, 2.50 mmol) were added. The mixture was stirred at 100 °C for 2 h before being cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through Celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (12 g silica cartridge, 0−100% EtOAc in hexane) to give 1-benzyl-5-(4-fluorophenyl)-1*H*-tetrazole (47.9 mg, 0.15 mmol, 60% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.54 (m, 2H), 7.37−7.31 (m, 3H), 7.21−7.09 (m, 4H), 5.61 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.44 to −107.60 (m). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.6 (d, $^1J_{C-F}$ = 253.2 Hz), 154.0, 133.9, 131.2 (d, $^3J_{C-F}$ = 8.8 Hz), 129.4, 129.0, 127.2, 120.1 (d, $^4J_{C-F}$ = 3.3 Hz), 116.7 (d, $^2J_{C-F}$ = 22.2 Hz), 51.6. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{12}FN_4$ 255.1046, found 255.1051. IR ν_{max} (neat): 3070, 2964, 2932, 2857, 1606, 1539, 1473, 1450 cm^{-1}. Analytical data are in agreement with the literature.[17]

1-Benzyl-5-(4-(trifluoromethyl)phenyl)-1H-tetrazole (2c). To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.250 mmol), (4-(trifluoromethyl)phenyl)boronic acid (71.2 mg, 0.375 mmol), and XPhos Pd G3 (10.6 mg, 0.013 mmol) was added toluene (2.5 mL). The vessel was purged with nitrogen, and cesium carbonate (163 mg, 0.5 mmol) and water (0.450 mL, 25 mmol) were

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added. The mixture was stirred at 100 °C for 6 h before being cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through Celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (24 g silica cartridge, 0−100% EtOAc in hexane) to give 1-benzyl-5-(4-(trifluoromethyl)phenyl)-1*H*-tetrazole (43.3 mg, 0.14 mmol, 56% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), 7.39−7.35 (m, 3H), 7.17−7.13 (m, 2H), 5.64 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.17 (s). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.7, 133.7, 133.4 (q, $^{2}J_{C-F}$ = 33.1 Hz), 129.50, 129.45, 129.1, 127.6, 127.2, 126.3 (q, $^{3}J_{C-F}$ = 3.5 Hz), 123.6 (q, $^{1}J_{C-F}$ = 272.6 Hz), 51.8. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{15}H_{12}F_3N_4$ 305.1014, found 305.1018. IR ν_{max} (neat): 3075, 3038, 2964, 1624, 1539, 1497, 1449, 1426 cm^{-1}. Analytical data are in agreement with the literature.[23]

*1-Benzyl-5-(4-methoxyphenyl)-1H-tetrazole (**2i**).* To a microwave vial containing 1-benzyl-5-bromo-1*H*-tetrazole (60 mg, 0.25 mmol), (4-methoxyphenyl)boronic acid (57.0 mg, 0.38 mmol), and XPhos Pd G3 (21.2 mg, 0.025 mmol) was added toluene (2.5 mL). The vessel was purged with nitrogen, and potassium carbonate (69.1 mg, 0.5 mmol) and water (0.045 mL, 2.50 mmol) were added. The mixture was stirred at 100 °C for 2 h before being cooled to room temperature. The mixture was then diluted with ethyl acetate, passed through Celite, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (24 g silica cartridge, 0−100% EtOAc in hexane) to give 1-benzyl-5-(4-methoxyphenyl)-1*H*-tetrazole (48.3 mg, 0.18 mmol, 72% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.0 Hz, 2H), 7.34−7.32 (m, 3H), 7.15−7.13 (m, 2H), 6.98 (d, J = 8.0 Hz, 2H), 5.60 (s, 2H), 3.84 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.0, 154.6, 134.2, 130.5, 129.3, 128.8, 127.2, 115.9, 114.8, 55.6, 51.4. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{15}H_{15}ON_4$ 267.1246, found 267.1250. IR ν_{max} (neat): 3081, 3027, 3006, 2958, 2937, 2841, 1611, 1581, 1477, 1446 cm^{-1}. Analytical data are in agreement with the literature.[23]

*5-Phenyl-1H-tetrazole (**3a**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), phenylboronic acid (79 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL, 50 mmol), toluene (5 mL), and ethanol (2.5 mL) to yield 5-phenyl-1*H*-tetrazole (47.7 mg, 0.32 mmol, 65% yield) as a white solid.

Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), phenylboronic acid (396 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1220 mg, 3.75 mmol), water (4.50 mL, 250 mmol), toluene (25 mL), and ethanol (12.5 mL) to yield 5-phenyl-1*H*-tetrazole (216 mg, 1.48 mmol, 59% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 16.84 (br. s, 1H), 8.07−8.01 (m, 2H), 7.64−7.56 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 155.3, 131.2, 129.4, 126.9, 124.1. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_7H_7N_4$ 147.0671, found 147.0671. IR ν_{max} (neat): 3054, 2974, 2911, 2834, 1652, 1608, 1563, 1485, 1465, 1409 cm^{-1}. Analytical data are in agreement with the literature.[24]

*5-(4-Fluorophenyl)-1H-tetrazole (**3b**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), 4-fluorophenylboronic acid (455 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1220 mg, 3.75 mmol), water (4.50 mL, 250 mmol), toluene (25 mL), and ethanol (12.5 mL) to yield 5-(4-fluorophenyl)-1*H*-tetrazole (245 mg, 1.48 mmol, 59% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 16.84 (br. s, 1H), 8.13−8.06 (m, 2H), 7.46 (app. t, J = 8.9 Hz, 2H). ^{19}F{^{1}H} NMR (376 MHz, DMSO) δ −108.98 (s). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 163.6 (d, $^{1}J_{C-F}$ = 249.0 Hz), 154.8, 129.4 (d, $^{3}J_{C-F}$ = 9.0 Hz), 120.9, 116.5 (d, $^{2}J_{C-F}$ = 22.3 Hz). HRMS (ESI)m/z: [M + H]$^+$ calcd for $C_7H_6FN_4$ 165.0576, found 165.0579. IR ν_{max} (neat): 3070, 2985, 2916, 2841, 1609, 1498, 1446, 1410 cm^{-1}. Analytical data are in agreement with the literature.[25]

*5-(4-(Trifluoromethyl)phenyl)-1H-tetrazole (**3c**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), (4-(trifluoromethyl)phenyl)boronic acid (123 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL, 50 mmol), toluene (5 mL), and ethanol (2.5 mL) to yield 5-(4-(trifluoromethyl)phenyl)-1*H*-tetrazole (47.1 mg, 0.21 mmol, 42% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 17.08 (br. s, 1H), 8.26 (d, J = 7.9 Hz, 2H), 7.98 (d, J = 7.9 Hz, 2H). ^{19}F{^{1}H} NMR (376 MHz, DMSO) δ −61.53 (s). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 155.3, 130.9 (q, $^{2}J_{C-F}$ = 32.1 Hz), 128.4, 127.7, 126.3, 123.8 (q, $^{1}J_{C-F}$ = 271.0 Hz). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_8H_6F_3N_4$ 215.0545, found 215.0547. IR ν_{max} (neat): 3070, 2990, 2916, 2852, 1682, 1573, 1506, 1441 cm^{-1}. Analytical data are in agreement with the literature.[24]

*5-(p-Tolyl)-1H-tetrazole (**3d**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), *p*-tolylboronic acid (88 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL, 50 mmol), toluene (5 mL), and ethanol (2.5 mL) to yield 5-(*p*-tolyl)-1*H*-tetrazole (41.2 mg, 0.26 mmol, 51% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 16.71 (br. s, 1H), 7.96−7.90 (m, 2H), 7.45−7.39 (m, 2H), 2.39 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 141.1, 129.9, 126.8, 121.3, 21.0, 1C not observed. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_8H_9N_4$ 161.0827, found 161.0828. IR ν_{max} (neat): 3043, 2964, 2917, 2848, 1612, 1570, 1504, 1432, 1404 cm^{-1}. Analytical data are in agreement with the literature.[24]

*5-(m-Tolyl)-1H-tetrazole (**3e**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), *m*-tolylboronic acid (88 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL, 50 mmol), toluene (5 mL), and ethanol (2.5 mL) to yield 5-(*m*-tolyl)-1*H*-tetrazole (21.3 mg, 0.13 mmol, 26% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 16.77 (br. s, 1H), 7.87 (s, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 155.3, 138.8, 131.8, 129.3, 127.4, 124.1, 20.9, 1C not observed. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_8H_9N_4$ 161.0827, found 161.0828. IR ν_{max} (neat): 3065, 2980, 2918, 2847, 1651, 1599, 1560, 1485, 1456, 1415, 1400, cm^{-1}. Analytical data are in agreement with the literature.[26]

*5-(o-Tolyl)-1H-tetrazole (**3f**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), *o*-tolylboronic acid (442 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1222 mg, 3.75 mmol), water (4.5 mL, 250 mmol), toluene (25 mL), and ethanol (12.5 mL) to yield 5-(*o*-tolyl)-1*H*-tetrazole (229 mg, 1.41 mmol, 57% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 16.63 (br. s, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.52−7.36 (m, 3H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 155.2, 137.1, 131.3, 130.7, 129.3, 126.2, 123.8, 20.4. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_8H_9N_4$ 161.0827, found 161.0827. IR ν_{max} (neat): 3065, 3027, 2964, 2921, 2847, 2714, 1654, 1606, 1561, 1484, 1464, 1404 cm^{-1}. Analytical data are in agreement with the literature.[24]

*5-(Naphthalen-2-yl)-1H-tetrazole (**3g**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (598 mg, 2.5 mmol), naphthalen-2-ylboronic acid (559 mg, 3.25 mmol), XPhos Pd G3 (63.5 mg, 75 μmol), Evonik P1071 Pd/C (266 mg, 250 μmol), cesium carbonate (1222 mg, 3.75 mmol), water (4.50 mL, 50 mmol), toluene (25 mL), and ethanol (12.5 mL) to yield 5-(naphthalen-2-yl)-1*H*-tetrazole (331 mg, 1.53 mmol, 61% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 16.96 (br. s, 1H), 8.66 (d, J = 0.8 Hz, 1H), 8.17−8.07 (m, 3H), 8.05−8.01 (m, 1H), 7.69−7.61 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 133.9, 132.6, 129.2, 128.6, 127.8, 127.8, 127.2, 126.9, 123.6, 121.6, 1C not observedHRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{11}H_9N_4$ 197.0827, found 197.0831. IR ν_{max} (neat): 3128, 3059, 2990, 2921, 2889, 2841,

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1635, 1609, 1564, 1510, 1417 cm^{-1}. Analytical data are in agreement with the literature.[24]

*5-(Pyren-1-yl)-1H-tetrazole (**3h**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), pyren-1-ylboronic acid (160 mg, 0.65 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), Evonik P1071 Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 0.75 mmol), water (901 μL, 50 mmol), toluene (5 mL), and ethanol (2.5 mL) to yield 5-(pyren-1-yl)-1*H*-tetrazole (37.6 mg, 0.11 mmol, 23% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 17.12 (br. s, 1H), 8.95 (d, J = 9.3 Hz, 1H), 8.49 (s, 2H), 8.44 (d, J = 2.9 Hz, 1H), 8.42 (d, J = 2.9 Hz, 1H), 8.39 (d, J = 9.4 Hz, 1H), 8.36 (d, J = 8.9 Hz, 1H), 8.30 (d, J = 8.9 Hz, 1H), 8.21−8.15 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 132.5, 130.7, 130.1, 129.2, 129.1, 128.8, 128.5, 128.1, 127.3, 127.2, 126.9, 126.4, 126.1, 125.0, 124.2, 124.0, 123.4. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{17}H_{11}N_4$ 271.0984, found 271.0988. IR ν_{max} (neat): 3022, 2921, 2847, 1577, 1454, 1421 cm^{-1}. Analytical data are in agreement with the literature.[27]

*5-(4-Methoxyphenyl)-1H-tetrazole (**3i**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), 4-methoxyphenylboronic acid (114 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), cesium carbonate (326 mg, 1.0 mmol), water (90 μL, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (36.3 mg, 34 μmol), and ethanol (2.5 mL) to yield 5-(4-methoxyphenyl)-1*H*-tetrazole (49.4 mg, 0.28 mmol, 60% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 7.98 (d, J = 8.9 Hz, 2H), 7.16 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H) 1H not observed (exchangeable). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 161.4, 128.6, 127.0, 116.3, 114.8, 55.4. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_8H_9ON_4$ 177.0776, found 177.0770. IR ν_{max} (neat): 3160, 3081, 3022, 2919, 2843, 1610, 1585, 1499, 1470, 1443, 1405 cm^{-1}. Analytical data are in agreement with the literature.[24]

*5-Phenethyl-1H-tetrazole (**3j**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), (*E*)-styrylboronic acid (111 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), cesium carbonate (326 mg, 1.0 mmol), water (90 μL, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (29.6 mg, 28 μmol), and ethanol (2.5 mL) to yield 5-phenethyl-1*H*-tetrazole (48.9 mg, 0.28 mmol, 77% yield) as a white solid. ^{1}H NMR (500 MHz, DMSO) δ 11.07 (br. s, 1H), 7.28−7.35 (m, 2H), 7.23−7.15 (m, 3H), 3.18 (t, J = 7.8 Hz, 2H), 3.06 (t, J = 7.7 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO) δ 155.4, 140.0, 128.4, 128.3, 126.3, 32.7, 24.6. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_9H_{11}N_4$ 175.0984, found 175.0977. IR ν_{max} (neat): 3030, 3007, 2992, 2972, 2922, 2857, 1560, 1491, 1454, 1425, 1408 cm^{-1}. Analytical data are in agreement with the literature.[28]

*5-([1,1′-Biphenyl]-2-yl)-1H-tetrazole (**3k**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), [1,1′-biphenyl]-2-ylboronic acid (150 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), cesium carbonate (326 mg, 1.0 mmol), water (90 μL, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (36.3 mg, 34 μmol), and ethanol (2.5 mL) to yield 5-([1,1′-biphenyl]-2-yl)-1*H*-tetrazole (24.1 mg, 0.11 mmol, 22% yield) as a white solid. Column chromatography (0−100% ethyl acetate in petroleum ether) following the hydrogenolysis step was required for this substrate. ^{1}H NMR (400 MHz, DMSO) δ 7.72−7.65 (m, 2H), 7.61−7.54 (m, 2H), 7.34−7.28 (m, 3H), 7.12−7.07 (m, 2H) 1H not observed (exchangeable). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 141.5, 139.2, 131.1, 130.6, 128.7, 128.2, 127.7, 127.4, 123.4, 2C not observed. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{13}H_{11}N_4$ 223.0978, found 223.0979. IR ν_{max} (neat): 3059, 2963, 2918, 2886, 2845, 2822, 1601, 1572, 1560, 1477, 1454, 1437 cm^{-1}. Analytical data are in agreement with the literature.[28]

*5-([1,1′-Biphenyl]-4-yl)-1H-tetrazole (**3l**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), [1,1′-biphenyl]-4-ylboronic acid (150 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), cesium carbonate (326 mg, 1.0 mmol), water (90 μL, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (27.3 mg, 26 μmol), and ethanol (2.5 mL) to yield 5-([1,1′-biphenyl]-4-yl)-1*H*-tetrazole (56.7 mg, 0.26 mmol, 53% yield) as a white solid. ^{1}H NMR (500 MHz, DMSO) δ 8.15 (d, J = 8.3 Hz, 2H), 7.91 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (app. t, J = 7.6 Hz, 2H), 7.43−7.40 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO) δ 155.0, 151.0, 142.7, 138.9, 129.1, 128.2, 127.6, 126.8, 123.1. HRMS (ESI) m/z: [M + H] calcd for $C_{13}H_{11}N_4$ 223.0978, found 223.0979. IR ν_{max} (neat): 3092, 3059, 3003, 2982, 2922, 2851, 1614, 1560, 1522, 1501, 1483, 1452, 1425 cm^{-1}. Analytical data are in agreement with the literature.[24]

*Methyl 4-(1H-Tetrazol-5-yl)benzoate (**3m**).* Synthesized in accordance with the general procedure using 1-benzyl-5-bromo-1*H*-tetrazole (120 mg, 0.5 mmol), (4-(methoxycarbonyl)phenyl)boronic acid (135 mg, 0.75 mmol), XPhos Pd G3 (12.7 mg, 15 μmol), cesium carbonate (326 mg, 1.0 mmol), water (90 μL, 5.0 mmol), toluene (2.5 mL), Evonik P1071 Pd/C (10.6 mg, 10 μmol), and ethanol (1.5 mL) to yield methyl 4-(1*H*-tetrazol-5-yl)benzoate (20.3 mg, 0.10 mmol, 27% yield) as a yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 8.19 (d, J = 8.6 Hz, 2H), 8.15 (d, J = 8.7 Hz, 2H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 165.6, 155.7, 145.3, 131.5, 130.1, 127.2, 52.4. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_9H_9N_4O_2$ 205.0720, found 205.0720. IR ν_{max} (neat): 3154, 3098, 3073, 3046, 3019, 2953, 2928, 2855, 1709, 1686, 1566, 1499, 1427 cm^{-1}. Analytical data are in agreement with the literature.[28]

*2,5-Diphenyl-2H-tetrazole (**4a**).* Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), phenylboronic acid (49 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 2,5-diphenyl-2*H*-tetrazole (36.7 mg, 0.17 mmol, 83% yield) as a white solid.

Synthesized in accordance with the general procedure using tetrazole **3a** (877 mg, 6.0 mmol), phenylboronic acid (1.5 g, 12 mmol), copper(I) oxide (43 mg, 0.3 mmol), and DMSO (10 mL) to yield 2,5-diphenyl-2*H*-tetrazole (1.2 g, 5.3 mmol, 88% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30−8.24 (m, 2H), 8.24−8.18 (m, 2H), 7.62−7.47 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.4, 137.1, 130.7, 129.8, 129.8, 129.1, 127.3, 127.2, 120.0. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{13}H_{12}N_4$ 223.0984, found 223.0986. IR ν_{max} (neat): 3066, 1595, 1530, 1497, 1470, 1447 cm^{-1}. Analytical data are in agreement with the literature.[29]

*N-(4-(5-Phenyl-2H-tetrazol-2-yl)phenyl)acetamide (**4b**).* Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), (4-acetamidophenyl)boronic acid (72 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield *N*-(4-(5-phenyl-2*H*-tetrazol-2-yl)phenyl)acetamide (49.7 mg, 0.18 mmol, 83% yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO) δ 10.32 (s, 1H), 8.18−8.13 (m, 2H), 8.09 (d, J = 9.0 Hz, 2H), 7.88 (d, J = 9.0 Hz, 2H), 7.63−7.58 (m, 3H), 2.11 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, MeOD) δ 162.4, 156.8, 132.3, 124.3, 122.3, 120.7, 118.9, 118.4, 112.1, 112.0, 14.5. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{15}H_{14}N_5O$ 280.1193, found 280.1196. IR ν_{max} (neat): 3265, 3144, 3073, 2961, 2926, 1667, 1605, 1557, 1531, 1510, 1468, 1452, 1418 cm^{-1}. Analytical data are in agreement with the literature.[29]

*2-(Naphthalen-2-yl)-5-phenyl-2H-tetrazole (**4c**).* Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), 2-naphthylboronic acid (69 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 2-(naphthalen-2-yl)-5-phenyl-2*H*-tetrazole (46 mg, 0.17 mmol, 84% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 2.0 Hz, 1H), 8.34−8.28 (m, 3H), 8.02 (d, J = 8.9 Hz, 1H), 7.98 (dd, J = 6.5, 2.7 Hz, 1H), 7.91 (dd, J = 6.3, 2.9 Hz, 1H), 7.62−7.48 (m, 5H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.4, 134.4, 133.5, 133.2, 130.7, 130.0, 129.1, 128.8, 128.1, 127.6, 127.5, 127.3, 127.2, 118.3, 118.0. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{17}H_{13}N_4$ 273.1140, found 273.1143. IR ν_{max} (neat): 3067, 3051, 2922, 1599, 1514, 1495, 1472, 1449 cm^{-1}

*5-Phenyl-2-(o-tolyl)-2H-tetrazole (**4d**).* Synthesized in accordance with the general procedure using tetrazole **3a** (29 mg, 0.2 mmol), *o*-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 5-phenyl-2-(*o*-tolyl)-2*H*-tetrazole (37 mg, 0.16 mmol, 78% yield) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29−8.22 (m, 2H), 7.70−7.65 (m, 1H), 7.57−7.49 (m, 3H), 7.48−7.38 (m, 3H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.1, 136.7, 133.3, 132.1, 130.7, 130.5, 129.1, 127.4,

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127.2, 127.1, 125.4, 18.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{13}N_4$ 237.1140, found 237.1141. IR ν_{max} (neat): 3051, 2959, 2920, 2853, 1585, 1530, 1497, 1468, 1450 cm^{-1}. Analytical data are in agreement with the literature.[13c]

*5-(4-Fluorophenyl)-2-phenyl-2H-tetrazole (**4e**).* Synthesized in accordance with the general procedure using tetrazole **3b** (39 mg, 0.24 mmol), phenylboronic acid (49 mg, 0.48 mmol), copper(I) oxide (1.7 mg, 12 μmol), and DMSO (2 mL) to yield 5-(4-fluorophenyl)-2-phenyl-2*H*-tetrazole (45 mg, 0.19 mmol, 78% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28−8.21 (m, 2H), 8.20−8.15 (m, 2H), 7.61−7.54 (m, 2H), 7.53−7.47 (m, 1H), 7.24−7.17 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ −109.57 (tt, J = 8.6, 5.3 Hz). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.6, 164.4 (d, $^1J_{C\text{-}F}$ = 250.9 Hz), 137.0, 129.9, 129.2 (d, $^3J_{C-F}$= 8.8 Hz), 123.6 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 120, 116.2 (d, $^2J_{C\text{-}F}$ = 22.0 Hz). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_{10}FN_4$ 241.0889, found 241.0891. IR ν_{max} (neat): 3082, 3069, 3045, 3026, 2924, 1597, 1541, 1495, 1491, 1474, 1458, 1423 cm^{-1}. Analytical data are in agreement with the literature.[30]

*N-(4-(5-(4-Fluorophenyl)-2H-tetrazol-2-yl)phenyl)acetamide (**4f**).* Synthesized in accordance with the general procedure using tetrazole **3b** (32.8 mg, 0.2 mmol), (4-acetamidophenyl)boronic acid (71.6 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 12 μmol), and DMSO (2 mL) to yield *N*-(4-(5-(4-fluorophenyl)-2*H*-tetrazol-2-yl)phenyl)-acetamide (42 mg, 0.14 mmol, 71% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 10.31 (s, 1H), 8.20 (dd, J = 8.5, 5.6 Hz, 2H), 8.08 (d, J = 8.9 Hz, 2H), 7.87 (d, J = 8.9 Hz, 2H), 7.45 (app. t, J = 8.8 Hz, 2H), 2.10 (s, 3H). ^{19}F NMR (471 MHz, DMSO) δ −109.54 − −109.62 (m). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 163.6 (d, $^1J_{C\text{-}F}$ = 248.1 Hz), 163.5, 141.0, 131.0, 129.0 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 123.1 (d, $^4J_{C\text{-}F}$ = 2.9 Hz), 120.7, 119.7, 116.5 (d, $^2J_{C-F}$ = 22.0 Hz), 24.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}FN_5O$ 298.1099, found 298.1101. IR ν_{max} (neat): 3310, 3277, 3208, 3150, 3088, 1665, 1609, 1541, 1508, 1466, 1423, 1414 cm^{-1}.

*5-(4-Fluorophenyl)-2-(naphthalen-2-yl)-2H-tetrazole (**4g**).* Synthesized in accordance with the general procedure using tetrazole **3b** (39.2 mg, 0.24 mmol), 2-naphthylboronic acid (68.8 mg, 0.42 mmol), copper(I) oxide (1.7 mg, 12 μmol), and DMSO (2 mL) to yield 5-(4-fluorophenyl)-2-(naphthalen-2-yl)-2*H*-tetrazole (10 mg, 0.04 mmol, 15% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 2.0 Hz, 1H), 8.35−8.26 (m, 3H), 8.04 (d, J = 9.0 Hz, 1H), 8.02−7.98 (m, 1H), 7.96−7.91 (m, 1H), 7.65−7.56 (m, 2H), 7.24 (dd, J = 13.6, 4.9 Hz, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ −109.41 to −109.65 (m). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.7, 163.4 (d, $^1J_{C-F}$ = 250.8 Hz), 134.4, 133.6, 133.2, 130.1, 129.3 (d, $^3J_{C-F}$ = 8.6 Hz), 128.8, 128.2, 127.7, 127.6, 123.6 (d, $^4J_{C-F}$ = 4.2 Hz), 118.4, 118.0, 116.3 (d, $^2J_{C-F}$ = 22.3 Hz). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{12}FN_4^+$ 291.1046, found 291.1046. IR ν_{max} (neat): 3061, 2953, 2922, 2851, 1607, 1603, 1539, 1510, 1476, 1460, 1447, 1423 cm^{-1}.

*5-(4-Fluorophenyl)-2-(o-tolyl)-2H-tetrazole (**4h**).* Synthesized in accordance with the general procedure using tetrazole **3b** (32.8 mg, 0.20 mmol), *o*-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 5-(4-fluorophenyl)-2-(*o*-tolyl)-2*H*-tetrazole (41.4 mg, 0.16 mmol, 81% yield) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.21 (m, 2H), 7.66 (dd, J = 7.7, 1.1 Hz, 1H), 7.50−7.37 (m, 3H), 7.25−7.18 (m, 2H), 2.43 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ −109.70 (tt, J = 8.6, 5.3 Hz). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.33 (d, $^1J_{C-F}$ = 250.7 Hz), 164.31, 136.6, 133.2, 132.1, 130.5, 129.2 (d, $^3J_{C-F}$ = 8.6 Hz), 127.1, 125.4, 123.7 (d, $^4J_{C-F}$ = 2.9 Hz), 116.3 (d, $^2J_{C-F}$ = 22.3 Hz), 18.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}FN_4^+$ 255.1046, found 255.1051. IR ν_{max} (neat): 3088, 2984, 2963, 2924, 2853, 1603, 1497, 1472, 1458, 1423 cm^{-1}

*5-(Naphthalen-2-yl)-2-phenyl-2H-tetrazole (**4i**).* Synthesized in accordance with the general procedure using tetrazole **3g** (39.2 mg, 0.20 mmol), phenylboronic acid (49 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 5-(naphthalen-2-yl)-2-phenyl-2*H*-tetrazole (46.4 mg, 0.17 mmol, 85% yield) as a beige solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.32 (dd, J = 8.5, 1.6 Hz, 1H), 8.26−8.22 (m, 2H), 8.02−7.97 (m, 2H), 7.92−7.87 (m, 1H), 7.61−7.54 (m, 4H), 7.51 (app. t, J = 7.4 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.5, 137.1, 134.5, 133.4, 129.81, 129.77, 128.93, 128.87, 128.0, 127.4, 127.1, 126.9, 124.6, 124.1, 120.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{13}N_4$ 273.1140, found 273.1143. IR ν_{max} (neat): 3051, 2930 2853, 1595, 1522, 1503, 1468, 1436 cm^{-1}.

*2,5-Di(naphthalen-2-yl)-2H-tetrazole (**4k**).* Synthesized in accordance with the general procedure using tetrazole **3g** (39.2 mg, 0.20 mmol), 2-naphthylboronic acid (69 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 2,5-di(naphthalen-2-yl)-2*H*-tetrazole (10.2 mg, 0.03 mmol, 16% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.72 (d, J = 1.7 Hz, 1H), 8.39 (dd, J = 4.5, 1.8 Hz, 1H), 8.37 (dd, J = 4.1, 1.8 Hz, 1H), 8.07 (d, J = 9.0 Hz, 1H), 8.05−7.99 (m, 3H;), 7.97−7.90 (m, 2H;), 7.66−7.55 (m, 4H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.6, 134.6, 134.5, 133.6, 133.4, 133.3, 130.1, 129.0, 128.9, 128.85, 128.2, 128.1, 127.7, 127.6, 127.4, 127.2, 126.9, 124.6, 124.2, 118.5, 118.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{21}H_{15}N_4$ 323.1297, found 323.1299. IR ν_{max} (neat): 3055, 3030, 1630, 1603, 1524, 1501, 1474, 1437 cm^{-1}

*5-(Naphthalen-2-yl)-2-(o-tolyl)-2H-tetrazole (**4l**).* Synthesized in accordance with the general procedure using tetrazole **3g** (39.2 mg, 0.20 mmol), *o*-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 5-(naphthalen-2-yl)-2-(*o*-tolyl)-2*H*-tetrazole (20.0 mg, 0.07 mmol, 35% yield) as a beige solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.32 (dd, J = 8.5, 1.6 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 8.00−7.97 (m, 1H), 7.93−7.88 (m, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.59−7.53 (m, 2H), 7.51−7.39 (m, 3H), 2.47 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.2, 136.7, 134.5, 133.4, 133.3, 132.1, 130.5, 129.0, 128.9, 128.0, 127.3, 127.07, 127.05, 126.9, 125.4, 124.7, 124.1, 19.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1297, found 287.1299. IR ν_{max} (neat): 3061, 2924, 2853, 1605, 1522, 1493, 1464, 1435 cm^{-1}

*2-Phenyl-5-(o-tolyl)-2H-tetrazole (**4m**).* Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), phenylboronic acid (49 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 2-phenyl-5-(*o*-tolyl)-2*H*-tetrazole (32.0 mg, 0.14 mmol, 68% yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO) δ 8.19−8.13 (m, 2H), 8.04 (dd, J = 7.6, 1.2 Hz, 1H), 7.73−7.66 (m, 2H), 7.64−7.59 (m, 1H), 7.50−7.36 (m, 3H), 2.64 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 164.9, 137.0, 136.2, 131.5, 130.4, 130.1, 129.2, 126.3, 125.6, 119.9, 21.2, 1C not observed. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{13}N_4$ 237.1135, found 237.1134. IR ν_{max} (neat): 3076, 3030, 2980, 2959, 2926, 1595, 1522, 1497, 1479, 1456, 1418 cm^{-1}.

*N-(4-(5-(o-Tolyl)-2H-tetrazol-2-yl)phenyl)acetamide (**4n**).* Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), (4-acetamidophenyl)boronic acid (71.6 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield *N*-(4-(5-(*o*-tolyl)-2*H*-tetrazol-2-yl)phenyl)acetamide (41.2 mg, 0.14 mmol, 71% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17−8.13 (m, 2H), 8.13−8.09 (m, 1H), 7.75 (d, J = 8.9 Hz, 2H), 7.56 (br. s, 1H), 7.43−7.31 (m, 3H), 2.71 (s, 3H), 2.23 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.6, 165.7, 139.3, 137.8, 133.0, 131.6, 130.3, 129.7, 126.3, 126.2, 120.7, 120.5, 24.8, 21.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}N_5O$ 294.1349, found 294.1351. IR ν_{max} (neat): 3294, 3269, 3211, 3148, 3075, 2957, 2926, 1661, 1611, 1535, 1510, 1481, 1450, 1414 cm^{-1}

*2-(Naphthalen-2-yl)-5-(o-tolyl)-2H-tetrazole (**4o**).* Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), 2-naphthylboronic acid (69 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 2-(naphthalen-2-yl)-5-(*o*-tolyl)-2*H*-tetrazole (17.3 mg, 0.06 mmol, 30% yield) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 2.0 Hz, 1H, 8.35 (dd, J = 9.0, 2.2 Hz, 1H), 8.18 (dd, J = 8.0, 1.5 Hz, 1H), 8.05 (d, J = 9.0 Hz, 1H), 8.03−7.99 (m, 1H), 7.97−7.91 (m, 1H), 7.65−7.57 (m, 2H), 7.45−7.35 (m, 3H), 2.77 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.9, 137.9, 134.5, 133.5, 133.3, 131.6, 130.3, 130.1, 129.8, 128.8, 128.2, 127.7, 127.5, 126.4, 126.3, 118.3, 118.0, 22.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1291, found

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287.1288. IR ν_{max} (neat): 3049, 3034, 2959, 2922, 2851, 1603, 1514, 1474, 1449 cm^{-1}.

*2,5-Di-o-tolyl-2H-tetrazole (**4p**).* Synthesized in accordance with the general procedure using tetrazole **3f** (32.0 mg, 0.20 mmol), *o*-tolylboronic acid (54 mg, 0.4 mmol), copper(I) oxide (1.4 mg, 10 μmol), and DMSO (2 mL) to yield 2,5-di-*o*-tolyl-2*H*-tetrazole (31.4 mg, 0.13 mmol, 63% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19−8.16 (m, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.49−7.34 (m, 6H), 2.72 (s, 3H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 165.4, 137.7, 136.7, 133.0, 132.1, 131.6, 130.3, 130.2, 129.7, 127.1, 126.4, 126.2, 125.3, 22.0, 19.1. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{15}N_4$ 251.1291, found 251.1290. IR ν_{max} (neat): 3063, 3032, 2961, 2924, 1607, 1584, 1520, 1495, 1476, 1452 cm^{-1}

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c00807.

General procedures, optimization experiments, and the NMR spectra of selected compounds (PDF)

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Notes

The authors declare no competing financial interest.

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